"This is High Time to Look into Peripubertal Ovarian Tumors"

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Summary of Introduction: The study titled *"This is high time to look into peripubertal ovarian tumors"* was conducted on the hypothesis that although it is uncommon to find ovarian tumors in peripubertal age but if present there are high chances of them being malignant. *Our objective was to know histopathological diagnosis of ovarian tumors in peripubertal age and to know frequency, histopathologic subtypes and prognosis of malignancies in these girls.*

Study Design: *Prospective and observational.*

Material and Methods: The study period was two years with effect from 01-07-07 to 30-06-09 with a follow up period of six months and was conducted in Lady Willingdon Hospital Lahore. All the patients between 10 – 21 years of age with a diagnosis of non inflammatory ovarian tumors were included and those with non ovarian pelvic masses were excluded. Sample size remained 40. A proforma was devised to collect data. Results were compiled and analyzed.

Results: 20% of the patients had malignancy, 87.5% was of germ cell origin and 12.5% was epithelial. All the malignancies were found in 12 – 16 year old patients. Abdominal pain was the commonest complaint. 80% patients had simple cysts, dermoids and endometriotic cysts. All were managed by open laparotomy. Outcome was not good in patients with immature teratoma.

Discussion: Key results, mean age, symptoms, outcome, future fertility and the future trends were discussed.

Conclusion: Ovarian malignancy at the peripubertal age is not a rare happening. A high index of suspicion for malignancy is required. There is a need to adhere to western standards of management and to enhance liaison between gynaecologists and the oncologists if we wish to achieve comparable outcomes in these unlucky patients.

Keywords: Peripubertal, adolescent, malignancy, adnexal mass, Ovarian germ cell tumours, cystadenoma, dermoid, teratoma, dysgerminoma, conservative, radical, chemotherapy, fertility.

Introduction

This study on *"This is high time to look into peripubertal ovarian tumors"* was conducted in Lady Willingdon Hospital Lahore. The significance of the study lies in the fact that although it is less common to find ovarian neoplasms in peripubertal age but when present there are high chances of them being malignant. Tender age of the patients, future fertility concerns and the inherent morbidity in a malignant disease triggered us to undertake the study. This is something which should not be ignored on human grounds. As our hospital is the biggest gynaecology hospital in the country, we expected to get reasonable sample size to draw robust conclusions on the frequency and outcomes of malignancies in peripubertal girls.

Results of our study showed that 20% of the patients had malignancy (8 out of 40), 87.5% of them were of germ cell origin (7out of 8) and only 12.5% were epithelial (1 out of 8). All the malignancies were in 12 – 16 year old patients. Abdominal pain was the commonest complaint. Out of germ cell tumors (GCTs), 4 had dysgerminoma (10% of total and 50% of malignancy), 3 had immature teratoma (7.5% of total and 37.5% of malignancy), and 6 patients (15%) had mature cystic teratoma. 18 patients (45%) had simple cysts and 8 (20%) had endometriotic cysts. All were managed by open laparotomy. Outcome was not good in patients with immature teratoma. There was lack of coordination between the gyanaecology and oncology departments.

On literature review it was observed that majority of the non inflammatory ovarian tumours during peripubertal age are simple physiological cysts, mature cystic teratomas and endometriomas. Malignancy in this age represents 2% of ovarian malignancy. Majority of these cancers are GCTs and less often they are epithelial in origin.[1] Immature teratoma, dysgerminoma endodermal sinus tumor, and mixed type account for the majority of these GCTs while embryonal carcinoma and polyembryoma are very few. Malignant GCTs are characterized by rapid growth and extensive intra abdominal spread. The symptoms and signs range from 1 day to 6 months with a median of 4 weeks, and the patients usually present with abdominal pain, palpable mass, abdominal distention and vaginal bleeding, and a very few with amenorrhea and precocious puberty.[2]

The size of these tumors varies from 7 cm to 40 cm with a median of 15 – 16 cm. The tumor is rarely bilateral (12 – 19%) Diagnosis depends mainly on age, abdominal symptoms, size and consistency of the tumor, and tumor markers AFP (alpha fetoproteins) and β – hCG (β subunit of human chorionic gonadotrophins). Surgery is the first step of management followed by adjuvant therapy, which depends on the histologic type. Dysgerminoma is very sensitive to

radiation while other germ cell tumors are not. Germ cell tumors are chemosensitive and currently combination chemotherapy is used. With this management approach, malignant GCTs show excellent prognosis.[3]

Aims and Objectives

1. To know histopathological diagnosis of ovarian tumors in peripubertal age.
2. To know frequency, histopathologic subtypes and prognosis of malignancies in peripubertal girls.

Material and Methods

Venue: Lady Willingdon Hospital Lahore.

Study Design: Prospective and observational.

Study Period: The study period was *two years* with effect from 01-07-07 to 30-06-09.

Follow up: Six months with effect from 01-07-09 to 31-12-09.

Sample size: 40.

Patient Selection: All the patients presenting to our hospital between 10 – 21 years of age with a clinical and ultrasound diagnosis of non inflammatory ovarian tumors were included in the study. Patients with a non ovarian pelvic / adnexal mass were excluded.

Variables to be studied: patient's age, clinical presentation, examination findings, *investigation reports including tumor markers, ultrasound scan and other imaging techniques,* operative details with *staging* in case of malignancy, post-operative recovery, histopathology, and chemotherapy. Follow up details, drop outs and outcomes were noted.

Outcome: Whether the patient is complaint and recurrence free at the end of follow up period.

Measures

Data Collection: A Proforma was devised to collect clinical data and results of investigation reports. Histopathology reports of all the patients were collected. Data was transferred to Microsoft excel and SPSS. 15 spread sheet. References were taken through internet from

www.pubmed,www.medscape and Medline search.

Data Analysis: Results were compiled from this data and were analyzed through SPSS 15.

Results

Out of 40 patients, 20 % had malignancy (8 out of 40) while 80% (32 out 40) had benign ovarian tumours. 87.5% of malignancy was of germ cell origin (7out of 8) and only 12.5% was epithelial (1out of 8). Out of germ cell tumors (GCTs), 4 had *histopathological diagnosis* of dysgerminona (10% of total and 50% of malignancy), 3 had immature teratoma (7.5% of total and 37.5% of malignancy), and 6 patients (15%) had mature cystic teratoma (benign dermoid cysts). Only 1 patient had an epithelial malignancy i.e. borderline serous cyst adenocarcinoma (1out of 8, 12.5% of malignancy). 18 patients (45% of total) had simple cysts out of which 16 were serous and two were mucinous cyst adenomas. and 8 (20% of total) had endometriotic cysts.

One patient with mature cystic teratoma was pregnant with an intact intrauterine singleton pregnancy of 28 weeks. All the patients except one had unilateral tumors. The only patient with bilateral masses had histopathological diagnosis of borderline serous cyst adenocarcinoma. Overall 4 patients with simple serous cysts and one with dermoid cyst had torsion.

The most *common presenting complaint* turned out to be pain abdomen of variable duration in all the 40 patients. All the 8 patients with malignancy presented with 3 complaints i.e. abdominal pain, mass abdomen and menstrual irregularity. One of them in addition had urinary retention. All the patients with simple cysts and dermoid cysts without torsion had a common complaint of pain abdomen for 2-6 months duration. Patients with torsion of cyst complained of sudden and severe pain abdomen of only 2-4 days duration. Whereas patients with endometriosis complained of dysmenorrhea, menstrual irregularity, and infertility in case of married patients.

All the ovarian tumors found in *the younger age group of 10 – 16 years* were malignant (8 out of 8) with a mean age of 14.25 years for dygerminoma and 15.00 years for immature teratoma. The only patient with borderline tumor was 16 years of age.

All the 40 patients were managed by *open laparotomy*. In all the cases of dysgerminoma, size was bigger than 16 × 16 cm and the masses were mainly solid with lobulated appearance. All cases of immature teratomas were solid and cystic with predominant ectodermal tissue on naked eye examination. All the malignancies were limited to one affected ovary with rupture of capsule in one patient of dysgerminoma and two patients of immature teratoma. All were managed by conservative surgical approach i.e. removal of mass, unilateral salpingoophorectomy with conservation of uterus and contra lateral ovary. Ascitic fluid came positive in the case of borderline serous cyst adenocarcinoma. No patient underwent 2nd look laparotomy.

There were no *postoperative complications* in any patient. Patients with simple cysts were discharged home with follow up dates. Patients with malignancy were referred to oncology along with follow up dates with us.

All the patients with simple, dermoid and endometriotic cysts had no complaints and no recurrence at the end of 6 months *follow up*. Patients with dygerminomas and a patient with borderline serous cyst adenocarcinoma showed good compliance and had been on chemotherapy as scheduled by oncologist and were complaint and recurrence free at the end of 6 months follow up. However all the 3 patients with immature teratoma did not complete chemotherapy and developed recurrence. They attended the oncologist with recurrence and were referred back to us for debulking. Their

families did not agree for debulking and never came for follow up again in spite of repeated calls from our side. One of them died 5 months after primary surgery while at home. The other 2 are still alive but are terminally ill at home.

Table 1: *Frequency, Percentages and Age distribution of tumors.*

Histopathologic Diagnosis	Frequency	Percentage Out of Total Patients	Percentage of Malignancy	Age Group
Dysgerminoma	4	10.0	50%	10 – 16 years
Immature teratoma	3	7.5	37.5%	
Borderline serous cyst adeno carcinoma	1	2.5	12.5 %	
Serous cyst adenoma	16	40.0	Benign	17 – 21 years
Mucinous cyst adenoma	2	5.0	Benign	
Dermoid cyst (mature cystic teratoma)	6	15.0	Benign	
Endometriotic cyst	8	20.0	Benign	
Total	40	100	8 (20% of 40 patients)	

Discussion

According to the results of our study, *20% of the patients (8 out of 40) had malignancy* this proved our hypothesis that although it is uncommon to find ovarian tumors in peripubertal age but if present there are high chances of them being malignant. *Out of malignant tumors, 87.5% were germ cell tumors* (7out of 8) and only 12.5% were epithelial (1out of 8). This is consistent with the national and international literature.[4,5]

According to results of our study, all the malignancy was found in 12 – 16 year age group with a mean age of 14.25 years for dygerminoma and 15.00 years for immature teratoma. This peak mean age is consistent with international literature. *Does it raise a question that younger is the age, higher is the chance of an ovarian tumour to be malignant?* In some studies dysgerminoma is the most common histologic subtype whereas in others immature teratoma is the most common subtype.[6] However if mature and immature teratoma are taken together then we can say that teratoma is the most common germ cell tumor in peripubertal age.[7]

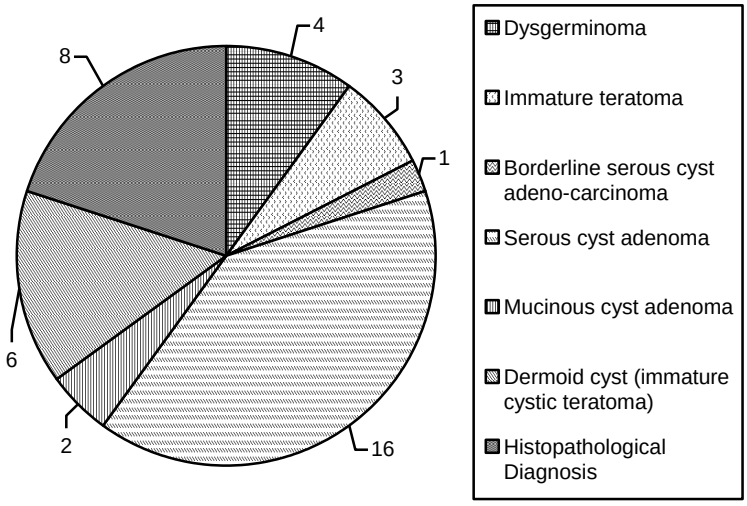

Fig. 1: *Histopathological Diagnosis.*

According to our study, the most *common presenting complaint* turned out to be pain abdomen of variable duration in all the 40 patients. All the 8 patients with malignancy presented with 3 complaints i.e. *abdominal pain, mass abdomen and menstrual irregularity.* This is again consistent with international literature.[8]

All the patients in our study were treated with *open laparotomy* and surgical approach was conservative. Non malignant symptomatic ovarian cysts are ideally managed by laparoscopy but facility was not available. Frozen section studies are ideally desirable but could not be done because of lack of facility. *These were our two major limitations.* The preferred surgical approach is conservative instead of radical surgery. Ovarian malignancies diagnosed in peripubertal young girls tend to be low-stage low – grade malignancies. This not only enables but also necessitates preserving the fertility. Conservative surgical approach after surgical staging includes cystectomy, unilateral salpingo-oophorectomy with conservation of contraleral ovary and uterus. Briefly, fertility saving surgery can be performed safely in germ cell, borderline and early stage epithelial ovarian tumours in selected cases.[9]

All the patients with malignancy in our study were referred to oncology department for chemotherapy. The outcome in 3 patients with immature teratomas remained poor as they did not complete chemotherapy and were lost in follow up. When they returned, the tumor had recurred

Table 2: *Major presenting complaints.*

		Number of Patients	Main Complaints
Malignancy (dysgerminoma, Borderline serous cyst adenoma and Immature teratoma)		8	Pain Mass abdomen, Menstrual irregularity. (just one patient complained of urinary retention)
Dermoid cysts	Without torsion	5	Pain 2 – 6 months duration
	With torsion	1	Pain 2 – 4 days duration
Simple cysts	Without torsion	14	Pain 2 – 6 months duration
	With torsion	4	pain 2 – 4 days duration
Endometriosis		8	Dysmenorrhea, menstrual irregularity (infertility in case of married patients)
100% Patients complained of pain abdomen			

extensively but even then patient's families refused debulking and then again got lost in the follow up and never turned back for further management. *One patient died 5 months after primary surgery and the other two are terminally ill at home*. This happened because of poor coordination between the clinicians and the patient's families. This is definitely not consistent with the international literature. Patients with dysgerminomas and borderline epithelial tumors showed good compliance. They have shown good outcomes with no recurrence after 6 months of follow up. Malignant GCTs and borderline epithelial tumours have excellent prognosis with optimal therapy. The majority of patients retain their reproductive function. In USA for example, most patients with Malignant GCTs, live a full life span. The 5 – year survival rate is 95%.[10,1] With a recurrence rate of 4.5% and a mortality rate of 3%, two other series confirmed an excellent prognosis for girls with ovarian germ cell cancer.[12,13]

It is high time to address the issue in our community as patients not only belong to a tender age group, there are important questions related to their future fertility and quality of life as well. Prognosis is better in the developed world as compared to the prognosis shown in our study. It can be improved by creating awareness in the community and by enhancing liaison between treating clinicians. A close collaboration between surgeons, histologists, radiologists and oncologists is essential to achieve good outcomes.[14]

The future holds several interesting possibilities. First, the rapid expansion of new laparoscopic equipment makes 4 minimally invasive surgery an area that is gaining importance in the treatment of simple ovarian cysts, dermoid cysts and endometriosis. Second, new developments in radiologic imaging will allow the clinicians to gain better insight into ovarian masses. Third, new but effective tumour markers and therapies should become available to assist in the diagnosis and treatment of ovarian cancers.

Conclusion

It was concluded that ovarian malignancy at the peripubertal age is not a rare happening. A high index of suspicion for malignancy is required if a patient in peripubertal age presents with an ovarian tumour. There is a need to adhere to western standards of management and to enhance liaison between gynaecologists and the oncologists if we wish to achieve comparable outcomes in these unlucky patients.

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